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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,798	08/24/2001	Nathan Karin	01/22078	3702

7590 07/01/2003

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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	9

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/856,798	Applicant(s) Karin
	Examiner Anne Marie Wehbé	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 22, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) *6, 7, and 12-33* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5, 8-11, and 34* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response received on 4/22/03 to the election/restriction requirement has been entered. Claims 1-34 are pending in the instant application. Applicant's election of the subject matter of Group I, claims 1-5, 8-11 and 34. The response does not indicate whether the election was made with or without traverse. However, since no arguments traversing the rejection appear in the response, the election has been treated as an election without traverse, and the restriction requirement has been made FINAL. Therefore, claims 6-7, and 12-33 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-5, 8-11, and 34 are currently under examination. An action on the merits follows.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: an application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

This application claims benefit to international application No. PCT/US99/26094 filed on 11/4/99. Applications that are filed on or after November 29, 2000, and that claim benefit to an

earlier-filed international application must include in the first sentence of the specification an indication of whether the international application was published in English under PCT Article 21(2) (regardless of whether the benefit for such application is claimed in an application data sheet). See 37 CFR 1.78(a)(2). The indication, as required by 37 CFR 1.78(a)(2), is missing. Applicant must supply the missing indication as an amendment to the specification in the reply to this Office action.

If applicant desires priority under 35 U.S.C. 120 or 35 U.S.C. 365(c) based upon a previously filed co-pending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. Since this application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and

the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-11 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating multiple sclerosis in a mammal comprising administering to said mammal polyclonal antibodies capable of neutralizing IGIF, does not reasonably provide enablement for the treatment of multiple sclerosis by administering any antibody which binds an interferon gamma inducing factor produced in said mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. In regards to claim 10 and 11, these composition claims are only included in this enablement rejection based on the recitation of intended use, "for inducing protective immunity against multiple sclerosis" in the preamble.

The claims as written read on the use of polyclonal, monoclonal, and humanized antibodies to treat multiple sclerosis. While claims 8-9 recite that the antibodies are neutralizing, claims 10-11 are not so limited. The specification states that polyclonal, monoclonal, and humanized antibodies can be used to treat multiple sclerosis. However, the specification fails to provide any actual description of any monoclonal antibody or humanized monoclonal antibody which is capable of "inducing protective immunity to multiple sclerosis" or of treating multiple sclerosis. The specification, while teaching that monoclonal antibodies may be made by screening polyclonal antibodies, and that humanized antibodies may be made according to teachings in the art, citing Wilder et al. and Carson et al., the specification fails to identify or provide the structural or chemical characteristics of any monoclonal or humanized antibody capable of neutralizing IGIF activity and further capable of treating multiple sclerosis. Please note that case law states that, "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1005 (CAFC 1997)

The working examples disclose polyclonal rabbit anti-rat IGIF IgG, which is capable of neutralizing the ability of IGIF to stimulate IFN-γ production in IGIF responsive cells, and which is further capable of reducing the severity of EAE in rats. The working examples do not teach any polyclonal anti-IGIF serum other than rabbit anti-rat IGIF IgG, or teach which antibodies contained in the polyclonal serum are responsible for neutralizing IGIF. The claims, however, are very broad and encompass monoclonal and humanized antibodies capable of binding to any

species of IGIF. While the state of the art at the time of filing was developed in making monoclonal and humanized antibodies, the prior art does not teach any structural features or properties that are capable of predicting whether an particular antibody would be capable of neutralizing the biological activity of the target antigen, or of treating any disease. Antibodies recognize particular epitopes on proteins. At the time of filing, the art is replete with examples of antibodies which bind to the target antigen without affecting activity of the target antigen. In view of the art recognized unpredictability of determining whether a particular antibody will be neutralizing and/or therapeutic, the identification of particular monoclonal or humanized antibodies against any species of IGIF which are capable of inhibiting the activity of IGIF, and further capable of treating multiple sclerosis would require substantial trial and error.

In addition, claims 8-9 read broadly on the use of an antibody which recognizes one species of IGIF to inhibit or neutralize IGIF activity is a animal of a different species. Neither the specification nor the prior art of record provides any guidance as to the level of epitope similarity between different species of IGIF. Further, the specification provides no guidance or evidence that antibodies against rat IGIF, for instance, are cross-reactive with human or canine IGIF. In view of the differences in protein sequences in protein homologues from different species, the skilled artisan would not have been able to predict without undue experimentation whether an antibody which bound to one species of IGIF would be capable of binding and neutralizing the activity of IGIF from a different species.

Therefore, in view of the breadth of the claims, the lack of guidance for monoclonal or humanized antibodies which are capable of neutralizing IGIF and/or treating multiple sclerosis, the lack of guidance for anti-IGIF antibodies which cross-react with IGIF from different species, the state of the art of antibodies at the time of filing, and the limitation of the working examples to polyclonal anti-IGIF, it would have required undue experimentation for the skilled artisan to practice the breadth of the claims as written. 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). It is also noted that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). Thus, since the specification does not enable the breadth of the claims as written, claims 8-11 and 34 fail to meet the requirements under 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 8-9, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites, "wherein said antibody is a neutralizing antibodies". An antibody is singular and antibodies is plural. Therefore it is unclear how a single antibody can encompass several "antibodies". Amendment of "antibodies" to "antibody" would overcome this grounds of rejection.

Claims 4, and 8-9 recites "neutralizing" or "neutralizing antibodies to" an "interferon gamma inducing factor in affecting cells to produce interferon gamma". The phrase "in affecting cells" is confusing since it is unclear whether the antibody is intended to "neutralize" IGIF in cells which produce interferon gamma, or whether the applicant intends to recite that the antibody neutralizes IGIF, wherein the IGIF causes cells to produce interferon gamma. As such the metes and bounds of the claims cannot be determined.

Claims 8-9 also recite a method "for treating an animal for inducing protective immunity against multiple sclerosis". The claim as written is confusing as it is unclear whether the applicant intends to claim two different outcomes from their method step, "treating an animal" and "inducing protective immunity against multiple sclerosis". The confusion originates in the double use of the word "for". Thus, the metes and bounds of the claim cannot be determined.

Claim 34 provides for the use of an antibody, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/ process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 34 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-2, 4, 8, 10, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Okamura et al. (1995) Nature, Vol. 378, 88-91. The applicant claims a polyclonal antibody capable of binding to interferon gamma inducing factor (IGIF, also known as IL-18), see claims 1-2. The applicant further claims said antibody which is a neutralizing antibody, see claim 4. In

addition, the applicant claims pharmaceutical compositions comprising said antibody, and the use of said antibody to treat multiple sclerosis, see claims 8, 10, 34.

In regards to claims 10 and 34, please note that the intended use of the antibodies for "treating multiple sclerosis" or for "inducing protective immunity against multiple sclerosis" has not been given patentable weight. The claims are product claims. Please note that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02). Thus, for the purposes of analysis under 35 U.S.C. 102, claims 10 and 34 read on a pharmaceutical composition comprising an antibody capable of binding an interferon gamma inducing factor.

Okamura et al. teaches neutralizing polyclonal anti-IGIF antiserum comprising anti-IGIF antibodies (Okamura et al., page 88, abstract, page 90, Figure 2, and page 91). Okamura et al. further teaches the use of the neutralizing anti-IGIF antibodies as a pharmaceutical composition to prevent endotoxin induced hepatic injury in mice (Okamura et al., page 91, Figure 4a-4c). Thus, by teachings all the elements of the claims as written, Okamura et al. anticipates claims 1-2, 4, 10, and 34.

Regarding claim 8, which recites a method of treating an animal for inducing protective immunity against multiple sclerosis comprising the step of administering to said animal an antibody capable of neutralizing IGIF, it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. In re Woodruff, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); In re Swinehart, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and Ex Parte Novitski, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Claim 8 recites a single step, the administration of a neutralizing anti-IGIF antibody to an animal. Since the claim recites "inducing protective immunity", the claim encompasses the administration of the antibody to animals who do not suffer from multiple sclerosis. Okamura et al. clearly teaches the administration of neutralizing anti-IGIF to mice in order to prevent hepatic injury resulting from endotoxin stimulation of IFN-γ. Since Okamura teaches the exact same method step as recited in the instant claims, Okamura et al. anticipates claim 8.

Claims 1-4 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al. (1997) J. Immunol. Meth., Vol. 206, 107-113. The applicant claims a polyclonal or monoclonal antibody capable of binding to interferon gamma inducing factor (IGIF, also known as IL-18), see claims 1-3. The applicant further claims said antibody which is a neutralizing antibody, see claim 4. In addition, the applicant claims, the use of said antibody to treat multiple sclerosis, see claim 34.

In regards to claims 34, please note that the intended use of the antibodies for "treating multiple sclerosis" has not been given patentable weight. The claims are product claims. Please note that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02). Thus, for the purposes of analysis under 35 U.S.C. 102, claims 34 reads on an antibody capable of binding an interferon gamma inducing factor.

Toniguchi et al. teaches anti-IGIF polyclonal antiserum, and monoclonal anti-IGIF antibodies (Toniguchi et al., page 108). Toniguchi et al. further teaches that the anti-IGIF antibodies are capable of neutralizing IL-18 dependant production of IFN-γ (Taniguchi et al., page 111, column 1 and Figure 1). Thus, by teachings all the elements of the claims as written, Taniguchi et al. anticipates claim 1-4 and 34.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okamura et al. (1995) Nature, Vol. 378, 88-91 in view of WO 91/09967 (1991), hereafter referred to as Adair et al. The applicant claims a humanized antibody capable of binding to interferon gamma inducing factor (IGIF, also known as IL-18), see claim 5, and a pharmaceutical composition comprising said humanized antibody, see claim 11.

In regards to claim 11, please note that the intended use of the antibodies for "inducing protective immunity against multiple sclerosis" has not been given patentable weight. The claim is a product claim. Please note that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand

alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02). Thus, for the purposes of analysis under 35 U.S.C. 102, claim 11 reads on a pharmaceutical composition comprising a humanized antibody capable of binding an interferon gamma inducing factor.

Okamura et al. teaches neutralizing anti-IGIF antiserum comprising anti-IGIF antibodies (Okamura et al., page 88, abstract, page 90, Figure 2, and page 91). Okamura et al. further teaches the use of the neutralizing anti-IGIF antibodies as a pharmaceutical composition to prevent endotoxin induced hepatic injury in mice (Okamura et al., page 91, Figure 4a-4c). Please note that Okamura was applied under 35 U.S.C. 102(b) above to independent claims 1 and 10 from which dependant claims 5 and 11 depend.

Okamura et al. differs from the antibodies recited in claims 5 and 11 by failing to teach a humanized antibody against IGIF. However, Okamura et al. does teach that the neutralizing anti-IGIF antibody is capable of inhibiting tissue injury in serious hepatitis caused by endotoxin, a condition similar to fulminant hepatitis in humans (Okamura et al., pages 89-90). Adair et al. supplements Okamura et al. by providing detailed instructions for making humanized antibodies (Adair et al., pages 6-64). Adair et al. further provides motivation for using a humanized antibody over a non-humanized antibody by teaching that antibodies

produced in rodents and in other non-human mammals generate undesirable HAMA responses in humans, limiting their re-administration, which can be avoided by using "humanized" antibodies (Adair et al., pages 1-3). Therefore, based on the motivation to use humanized antibodies over natural antibodies in humans provided by Adair et al., and the motivation to use anti-IGIF antibodies to prevent hepatitis, including fulminant hepatitis in humans, provided by Okamura et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to make a humanized version of the anti-IGIF antibody taught by Okamura et al.. Further, based on the detailed instructions provided by Adair et al. and the high level of skill in the art of molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in making a humanized anti-IGIF antibody.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Fri from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-

0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER